Supporting policy to improve delayed diagnosis of cancer in Nigeria

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Abstract

The majority of people with cancer present in late stage (Stage III or IV) in Sub Saharan Africa, resulting in poor outcomes. In Nigeria, over three-quarters of common curable cancers present late, compared to 35% in high-income countries. Early detection, and referral to surgical and treatment centres for first line treatment could potentially improve outcomes.

Aim: To investigate delays to cancer care in Nigeria

Work packages:

1. Elicit patients’ accounts from first noticing a bodily change to the point of resolution where patients receive treatment, or are informed the cancer is not treatable (n=480)

2. Engage with policy makers to share evidence and inform the development of interventions to improve detection and treatment of cancer

Our research will focus on four types of cancer:

· breast
· colorectum
· head and neck
· cervix

We will explore the patient journey according to the three stages to diagnosis outlined in the WHO guide to early cancer diagnosis, focusing on the duration and causes of delay from first symptom to treatment.

Introduction

Cancer is a leading cause of death worldwide; in 2020 there were nearly 10 million deaths in 2020, accounting for nearly one in six deaths. (1) Low and middle-income countries (LMICs) have a substantial and growing cancer burden, with a significantly higher cancer mortality than that of high-income countries. (2) The majority of people with cancer present in late stage (Stage III or IV) in Sub Saharan Africa (SSA) (3) – for example a median of 75% for breast cancer across studies in a 2016 systematic review. (4) Late presentation is associated with poor prognosis, increased mortality and much lower cure rates for many cancers. (5, 6) A systematic review showed that increased time to diagnosis and treatment for symptomatic cancer is associated with poorer outcomes for cancers of the breast, colorectum, head and neck, testes, and for melanoma (6) in terms of mortality and quality of life.
Nigeria has a population of 219 million, larger than that of the UK, France and Germany combined. Cancer incidence is rising in Nigeria as people live longer and adopt new lifestyles.\(^{(7)}\) In Nigeria, over three-quarters of common curable cancers present late versus about 35% in High-Income Countries (manuscript submitted for publication). Hospital case notes of urban dwellers identified from the Nigerian Cancer registry with breast, uterine cervix, colorectum or prostate cancer, showed that over two-thirds (71.4% in 2012-13 and 71.8% in 2017-18) presented in stages 3 or 4 (publication forthcoming).

Cancer is a high priority for the government in Nigeria and facilities for surgical treatment of common cancers are widely available in surgical centres. Early detection and referral to these centres for first line treatment could potentially improve prognosis and outcomes for patients with common cancers which are treatable (usually by means of excision). It is therefore important to better understand barriers to diagnosis and treatment using contextually appropriate tools in order to inform policy and develop interventions to improve pathways to cancer care.

The first step in this process is to discover why cancers present late. This protocol describes how, through our strong links with stakeholders such as health authorities and patients, we will investigate reasons for delays to cancer care in Nigeria. This information will provide early findings for policymakers and inform development of targeted interventions for roll-out and evaluation. By working with Ministries of Health, communities, and health professionals, we will be able to provide initial evidence to shape emerging policy.

Our research will focus on cancers of the following four types: 1) breast, 2) colorectum, 3) head and neck, and 4) cervix. These cancers are common and they can be cured if treated at an early stage and they present symptoms while still at an early stage.

We will interview cancer patients to elicit accounts of their journey to quantify the delays and barriers at each stage from their perspective (described below). This will provide preliminary evidence for policymakers to design interventions for evaluation in a much larger grant application. For example, if we find that 80% of the delay in the case of colon cancer is in presentation, but the percentages are reversed for head and neck cancer, then patient/public education is the remedy in the first and clinician education in the second.

It is likely we will observe bottlenecks at different stages. For example, a study similar to the one proposed here but carried out in Tanzania found that 45% of delay took place between first symptom and first presentation at formal health services while 55% occurred within the health services themselves \(^{(8)}\). Our findings will also shed light on barriers. For example, traditional healers are a barrier in some places but not in others \(^{(9-12)}\). Religious authorities are a barrier to referral in some places \(^{(13)}\).

Theoretical framework
We will draw from the WHO (14) and Aarhus (15) methods for studies of early cancer diagnosis. These methods are based on retrospective accounts from consecutive consenting patients with specific cancer diagnoses. The WHO guide to early cancer diagnosis (14) defines early diagnosis as the early identification of cancer in patients who have symptoms of the disease. We will explore the patient journey from first noticing bodily changes to the point of resolution where patients receive treatment, or are informed the cancer is not treatable. We will explore the patient journey according to the three stages to diagnosis outlined in the WHO guide to early cancer diagnosis as outlined below (14):

· Stage 1: awareness of symptoms and accessing care - We will explore symptom appraisal and health seeking behaviour to the first time they present to a formal healthcare professional. The delay associated with this stage is referred to as ‘access delay’.

· Stage 2: Clinical evaluation, diagnosis and staging - We will explore how the patient navigates the health system from first presentation to healthcare professional to receiving a histological diagnosis of cancer and referral for treatment. The delay associated with this stage is referred to as ‘diagnostic delay’.

· Stage 3: Access to treatment – from point of diagnosis to resolution (as defined above). The delay associated with this stage is referred to as ‘treatment delay’.

Aims and objectives

Our aim is to better understand delays on the pathway to care and the causes of these delays. Our objectives are to:

1. Estimate the duration of delay at stages 1,2 and 3 of the pathway

2. Elicit barriers and facilitators that patients encounter at each stage

We will seek to break the first stage (bodily change to first presentation to a formal health provider) into the pre-contemplative and contemplative stages. This distinction follows Anderson's observation that people may observe a cancer for some time before consciously assimilating its importance.

We will also decompose stage two into delays in referral from primary care to specialist care and delays in the specialist care itself. Some people refer themselves directly to specialist care, and we will record subsequent delays in these patients, including noting visits to other providers prior to diagnosis and treatment. Some people consult traditional healers after they have been in contact with specialist services (8) and we will therefore enquire about such visits. Some people may die of cancer before diagnosis and this ‘survivor-bias’ means findings may err on the side of over-estimating proportions presenting early.

Reagents
### Equipment

### Procedure

1. **Stakeholder consultation** - We have held community-based workshops (one in Ibadan and one in Kano) in preparation of this updated protocol. We invited policymakers, community leaders and patient groups (such as Cancer and Palliative Support Groups). The workshops took place at the University College Hospital Ibadan (24\textsuperscript{th} April 2023) and Aminu Kano Teaching Hospital (26\textsuperscript{th} April 2023). We sought advice on the study as a whole and co-produced the final version of the strategy to recruit participants.

The group advised on culturally sensitive issues that consider local beliefs and values. They identified factors to bring out in subsequent interviews – for example the role of traditional healers and religious leaders and advised on sensitive issues, such as interviewing people who cannot be cured, to ensure that the encounter is a positive experience for participants and support the development of research materials such as consent forms to ensure that they are culturally appropriate and accessible.

2. **Data collection (work package 1):** - Semi-structured interviews of 80 consecutive people per selected cancer (cancers of the breast, colorectum, head and neck, cervix) \(n=480\) patients in total. We have selected these four cancers as they have the potential of being diagnosed early and they are the most common cancers where the difference in outcome by stage of diagnosis is large.

**Eligibility criteria**

The inclusion criteria are:

- Patients with a first histological confirmed diagnosis of breast, colorectum, head and neck, cervical cancer
- Aged \(\geq\) 18 years
- Ability to provide informed consent

The exclusion criteria are:

- Patients without capacity to give informed consent
- Diagnosis of a cancer secondary to a primary cancer
- Patients who are acutely ill or receiving end of life care

See Figure 1. Flowchart of work package 1.
3. Study setting

We will conduct our study in the North (Kano) and South West (Ibadan) of Nigeria. The University College Hospital Ibadan will be the recruiting centre for Ibadan. The Aminu Kano Teaching Hospital will be the recruiting centre for Kano, with Murtala Muhammed Specialist Hospital and Muhammad Abdullahi Wase (Nassarawa) Hospital as additional study sites in Kano.

4. Participant recruitment

We will recruit consecutive patients from each recruitment centre as they are identified until the target number of participants is met for each cancer. Recruitment of participants from hospital has been used in high-income countries and low and middle-income countries (LMIC), including Ibadan with respect to breast cancer. (9)

The recruitment process will vary slightly from site to site but will hew to the schedule in Figure 2. (Flowchart for identification and recruitment of participants). The timepoints of interest are detailed in Table 1. (Supplementary file)

5. Interview schedule

The interview schedule is included in the supplementary information. The interview plan was devised to measure delays by stage and sub-stage and to explore the reasons for delay. Questions will elicit information on each stage of the WHO steps to early cancer diagnosis pathway drawing from the literature of validated instruments (15,16). The interviews will explicate the pathway for each person (people may make multiple attempts to access care and use alternative / traditional pathways) and identify the duration of each stage of the pathway and delays at each stage.

i. Measurement of delay We now describe the steps we will take to get to the best estimate of these dates.

We will use calendar methodology (17) to develop a calendar using key time points such as Easter, Christmas, New year, Ramadan as well as more local time points such as national and elections, festivals and seasons to use as a recall aid. The interviewing researchers will ensure trustworthiness of the data by checking back the sequence and time points with interviewees and exploring any inconsistencies. By recruiting patients as close as possible to the point of diagnosis we reduce the risk of recall bias.

We will tease apart, as much as possible, the gap between first noticing a body change and recognising that this might be a serious indication of disease (pre-contemplative stage), and the subsequent gap
between realising the change may be important and reaching an allopathic practitioner. Eliciting the duration of delay by stage will be facilitated by reference to dates in their personal lives and external events. We will measure median, interquartile range and, as recommended by WHO,(2) the 75th and 90th centiles and relate these to the WHO reference standard of 90 days from symptom to treatment. Some people may die of cancer before diagnosis and this ‘survivor-bias’ means findings may err on the side of over-estimating proportions presenting early.

ii. Barriers to access We shall identify causes of delayed presentation that are specific to a particular context and those that are shared. The role of other community members (example health workers, traditional healers) will be explored to try and understand the thought process. We will also elicit views about prognosis, therapy, effectiveness of therapy and local providers (e.g. quality, attitude). Important findings gleaned from accounts of patients’ experiences include the attitude of staff and the perception of the quality of the service which would propel interventions that would have benefit for all cancer patients and those with other conditions. We shall elicit the patient’s perspective regarding the reasons for any delay and what could be done about it.

6. Data analysis

The qualitative data will be analysed using framework analysis(18). Two researchers will read the same set of interviews for each cancer to identify emerging themes and together develop a thematic framework for coding the interviews. All interviews will then be coded according to the thematic framework, aided by Nvivo software. Interpretation will be by discussion and consensus between the study team. Data analysis will be iterative, occurring as data collection progresses.

We will identify themes within each of the three stages to early diagnosis for each cancer, identify the most important delays that impact on time to accessing treatment, and evaluate the reasons for the delays. Quantitative delays, for each of the three stages will be extracted from transcripts.

We will estimate median, interquartile range and, as recommended by WHO,(14) the 75th and 90th centiles and relate these to the WHO reference standard of 90 days from symptom to treatment.

7. Provide preliminary evidence to policymakers (work package 2)

Local and national policymakers will engage in a structured meeting with each of our site teams as findings emerge to discuss implications and to co-design solutions. A national policy meeting will be held will be held in the final month of the study.
Troubleshooting

Time Taken

The study will be conducted over sixteen months. The first four months will be used to co-design the study protocol and gain the necessary regulatory approvals. Engagement with policy makers will start in month one and repeated every 6 months for the duration of the study. Participant recruitment for work package 1 will start at Month 4. All data will be collected by Month 11, and the National Policy meeting will held in month 16.

Anticipated Results

References


**Figures**
Figure 1. Flowchart for work package 1

Community based workshop

Centre 1: Ibadan
University College Hospital

Centre 2: Kano
Aminu Kano Teaching Hospital, Murtala
Muhammad Specialist Hospital,
Muhammad Aminu Wase Hospital

Site staff identify patients meeting the eligibility criteria:
- Patients with a first diagnosis of cancer of the breast, colorectum, head and
  neck or cervix
- Aged ≥18 years
- Ability to provide informed consent

Screen to confirm suitability

Invite and recruit suitable patients (informed consent)

Conduct patient interviews
Ibadan - 240 patients with cancer
- Breast, n=60
- Colorectum, n=60
- Head and neck, n=60
- Cervix, n=60

Kano - 240 patients
- Breast, n=60
- Colorectum, n=60
- Head and neck, n=60
- Cervix, n=60

Data analysis
1. Thematic analysis according to WHO stages to early cancer diagnosis
   - Awareness and accessing care
   - Clinical evaluation, diagnosis and staging
   - Access to treatment
2. Quantitative presentation of delays to diagnosis at each stage
   - Access delay
   - Diagnostic delay
   - Treatment delay

Figure 1

Figure 1. Flowchart for work package 1
Figure 2. Flowchart for identification and recruitment of participants.
Figure 3. Example estimation of median delay

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.
- Table1.docx
- Researchinstrument.docx